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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/661,804	09/12/2003	Gerold Schuler	1430/16	8361

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EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

MAIL DATE	DELIVERY MODE
03/31/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/661,804	SCHULER ET AL.	
	Examiner	Art Unit	
	CELINE X. QIAN	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12 and 24-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12 and 24-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 12, 24-32 are pending in the application.

This Office Action is in response to the Amendment filed on 1/8/08.

Response to Amendment

The rejection of claims 12, 24-32 under 35 U.S.C.112 1st paragraph in light of the amendment.

The rejection of claims 12, 24-32 under 35 U.S.C.103 (a) is maintained for reason set forth of the record mailed on 8/8/07 and further discussed below.

Response to Arguments

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12, 24-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jonuleit et al. and Takahashi et al.

Jonuleit et al. disclose a method that of identify, monitor and/or remove CD4+CD25+ cells from human blood by contacting the blood with CD4 and/or CD25 and/or CTL-A4 specific antibodies (see page 1214, 2nd col., 4th paragraph, lines 1-6, and Figure 4). Jonuleit et al. further disclose that CD4+ T cells are removed from the cord blood (page 1214, 2nd col., 4th paragraph, lines 1-3). Jonuleit et al. also disclose that the purification is carried out using antibodies attached to beads (page 1214, 2nd col., 4th paragraph, last two lines). Lastly, Jonuleit et al.

disclose said method wherein the cells are stimulated with dendritic cells (see page 1215, 1st paragraph, lines 2-4). Further, Jonuleit et al. disclose analyzing expression of CTL-4.

However, Jonuleit et al. does not teach that no stimulation of DC when isolating said cells.

Takahashi et al. teach CD25+CD4+ cells are isolated from lymphoid organs of mouse by using CD25 and CD4 antibodies with stimulation of cytokines and dendritic cells (see page 304, Figure 1 and legend).

It would have been obvious to one of ordinary skill in the art to develop a method of identifying, monitoring, and removing CD4+ CD25+ regulatory T cells from human blood by using ligands specifically binds to the CD4 and CD25 based on the combined teaching of Jonuleit and Takahashi et al. Jonuleit et al. teach the CD4+ cells are first isolated from cord blood and stimulated with DC and then CD25 antibody is used to purify the CD4+CD25+ population. Takahashi et al. teach that CD25+CD4+ T cells are isolated from spleen cell suspension by using CD4 and CD25 antibody without stimulation of the cells with cytokine or dendritic cells. It is clear from the teaching of both references that T cells that are CD4+ CD25+ can be isolated from a mixed population of cells, either from blood or lymphoid tissue, by using CD4+CD25+ antibodies. Stimulation of the mixed cell population with cytokine or dendritic cell does not affect that ability of CD4 and CD25 antibody to bind to CD4 and CD25 surface antigen on such cells, thus isolation CD4+CD25+ by using CD4 and CD25 binding ligand without stimulation of cytokine or dendritic cells would yield the predictable result. Thus, it would have been obvious to one of ordinary skill in the art to identify, monitor and removing

CD4+CD25+ cells from blood by using binding ligands to such surface molecules without stimulation with cytokine or dendritic cells.

In response to this rejection, applicants argue that the claimed invention has unexpected results. Applicants argue that neither Jonuleit and Takahashi teach the presence of human blood comprises CD4+CD25+ regulatory T cells, which is required by step a. Applicants argue that without the knowledge that such cells exist in human blood, one of ordinary skill in the art would not have found it obvious to contact human blood with the claimed antibodies, and would not expect to identify, monitor and/or remove CD4+CD25+ regulatory T cells from human blood. Applicants argue that Jonuleit does not teach human blood comprise CD4+CD25+ regulatory T cells, the cells identified in this article is result from stimulation. Applicants assert that Takahashi is silent whether human blood comprises CD4+CD25+ regulatory T cell as mouse does. Applicants further assert that the claimed invention is characterized by unexpected result. Applicants assert that T cell exhibiting CD4+CD25+ were known for over a decade prior to the present invention, but were misinterpreted as being conventional memory cells, and all that time no CD4+CD25+ regulatory cells were identified in human. Applicants assert that the discovery of a known population of cells that has different character is an unexpected result. Applicants thus conclude that the claimed invention is not obvious in view of the prior art.

This argument has been fully considered but deemed unpersuasive. The instant claims are drawn to a method of identifying, monitoring and/or remove CD4+CD25+ regulatory T cells from human blood comprising two simple steps: a) contacting human blood comprising CD4+CD25+ regulatory T cells with ligands specifically binding to the CD4 and CD25 and/or CTLA-4 entities on the T cell; and b) identifying, monitoring and/or removing said CD4+CD25+

regulatory T cells from the human blood. The claimed method itself does not indicate any unpredictable result because human blood inherently comprises CD4+CD25+ regulatory T cells, and adding the limitation of "human blood comprising CD4+CD25+" does not change the claim scope or indicate any unexpected result. It is true that neither Takahashi nor Jonuleit teach contacting human blood directly with CD4+CD25 antibody without stimulation. However, for reason discussed in the rejection, it would have been obvious to an ordinary artisan to try to identify whether such cells exist in human blood as that in murine model and use antibody available to identify such cells. A person of ordinary skill in the art, upon reading the Takahashi reference would have recognize the desirability of finding out the same population of T cells exists in human blood. In fact, as admitted by Applicants, there is a long felt need to identify human counterpart cells. To use antibody of CD4 and CD25 as disclosed by Jonuleit to identify such cells in human blood is one of the finite number of method a skilled artisan would try to identify such cells in human blood. As such, the claim would have been obvious because a person of ordinary skill has good reason to pursue the known options within his or her technical grasp, in the instant case, to practice the method of contacting human blood with the antibodies and identify, monitor and/or remove CD4+CD25+ regulatory cells with anticipated results of finding those cells. In fact, Applicants have admitted that this population of cells has already been known in the art for over a decade. The novelty of the instant invention or the unexpected result of the invention is actually to identify the characteristic/function of the cell being regulatory T cell rather then conventional memory cells. However, since the claimed method is not directed to such method, and the recited method steps do not include any step that would tell the difference between the cells being either memory cell or regulatory T cell, the claimed

invention is simply drawn to a method that is able isolate T cell expresses both CD4 and CD25. Therefore, for reason discussed in the previous office action and above, this rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CELINE X. QIAN whose telephone number is (571)272-0777. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joe Woitach Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Celine X Qian Ph.D./
Primary Examiner, Art Unit 1636